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 DICTIONARY FILE UPDATES: 18 NOV 2009 HIGHEST RN 1192748-82-5

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TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

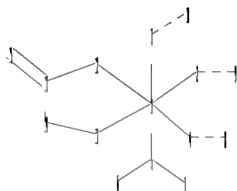
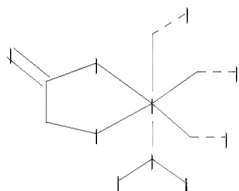
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chain nodes :
 2 3 4 5 6 7 8 9 10 15
 ring nodes :
 1 11 12 13 14
 chain bonds :
 1-2 1-3 1-4 1-5 2-9 3-10 4-8 5-6 5-7 13-15
 ring bonds :
 1-11 1-12 11-14 12-13 13-14
 exact/norm bonds :
 1-11 1-12 2-9 3-10 4-8 11-14 12-13 13-14 13-15
 exact bonds :
 1-2 1-3 1-4 1-5 5-6 5-7

Match level :
 1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
 10:CLASS 11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS

L1 STRUCTURE UPLOADED

=> d his

(FILE 'HOME' ENTERED AT 14:33:52 ON 19 NOV 2009)

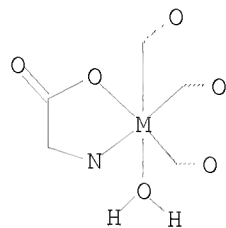
FILE 'REGISTRY' ENTERED AT 14:34:16 ON 19 NOV 2009

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 14:34:40 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 2368 TO ITERATE

84.5% PROCESSED 2000 ITERATIONS 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**

PROJECTED ITERATIONS: 44441 TO 50279

PROJECTED ANSWERS: 1 TO 88

L2 1 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 14:34:47 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 46866 TO ITERATE

100.0% PROCESSED 46866 ITERATIONS 30 ANSWERS
SEARCH TIME: 00.00.02

L3 30 SEA SSS FUL L1

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	185.88	186.10

FILE 'CAPLUS' ENTERED AT 14:34:53 ON 19 NOV 2009

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FILE COVERS 1907 - 19 Nov 2009 VOL 151 ISS 21
FILE LAST UPDATED: 18 Nov 2009 (20091118/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

CAPLUS now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s 13

L4 10 L3

=> d 1-10 bib abs

L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2009:9634 CAPLUS

DN 150:185528

TI Synthesis and Characterization of Nonsteroidal-Linked $M(\text{CO})_3^+$ ($M = {}^{99m}\text{Tc}$, Re) Compounds Based on the Androgen Receptor Targeting Molecule Flutamide
AU He, Haiyang; Morely, Jennifer E.; Silva-Lopez, Elsa; Bottenus, Brienne; Montajano, Maribel; Fugate, Glenn A.; Twamley, Brendan; Benny, Paul D.
CS Department of Chemistry, Washington State University, Pullman, WA, 99164, USA

SO Bioconjugate Chemistry (2009), 20(1), 78-86

CODEN: BCCHE5; ISSN: 1043-1802

PB American Chemical Society

DT Journal

LA English

OS CASREACT 150:185528

AB Androgen receptors are overexpressed in most primary and metastatic prostate cancers. A series of single photon emission computed tomog. imaging agents (SPECT) utilizing the organometallic radioactive imaging species, $\text{fac-}^{99m}\text{Tc}(\text{OH}_2)_3(\text{CO})_3^+$, were prepared on the basis of the structure of Flutamide, a potent nonsteroidal antiandrogen prostate cancer drug. Novel bifunctional chelate-linked Flutamide analogs were prepared using a newly developed universal alkylating reagent, 2-bromo-N-[4-nitro-3-(trifluoromethyl)phenyl]-acetamide, 1. From compound 1, several ligands (i.e., cysteine 2, histidine 5, imidazole 3) were conjugated to the flutamide derivative to yield targeting ligands capable of either tridentate or monodentate coordination in a "2 + 1" complex. $\text{fac-Re}(\text{CO})_3^+$ complexes were prepared and characterized with the functionalized conjugates to yield $\text{fac-Re}(\text{CO})_3(2\text{-amino-3-(1-(2-(4-nitro-3-(trifluoromethyl)phenylamino)-2-oxoethyl)-1H-imidazol-4-yl) propanoate})$, 4, $\text{fac-Re}(\text{CO})_3(2\text{-(S-cysteinyl)-N-[4-nitro-3-(trifluoromethyl) phenyl]-acetamide})$, 6, and $\text{fac-Re}(\text{CO})_3(\text{picolinate})(2\text{-(1H-imidazol-1-yl)-N-[4-nitro-3-(trifluoromethyl)phenyl]-acetamide})$, 7. The corresponding radioactive ${}^{99m}\text{Tc}$ analogs were prepared and stability studies of the radioactive compds. were also conducted.

OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:579127 CAPLUS
DN 147:183808
TI Cell-specific and nuclear targeting with [M(CO)3]+(M = 99mTc, Re)-based complexes conjugated to acridine orange and bombesin
AU Agorastos, Nikos; Borsig, Lubor; Renard, Anabelle; Antoni, Philipp; Viola, Giampietro; Spingler, Bernhard; Kurz, Philipp; Alberto, Roger
CS Institute of Inorganic Chemistry, University of Zuerich, Zurich, 8057, Switz.
SO Chemistry--A European Journal (2007), 13(14), 3842-3852
CODEN: CEUJED; ISSN: 0947-6539
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
OS CASREACT 147:183808
AB Receptor-specific nuclear targeting requires trifunctional metal complexes. We have synthesized [M-(L2-pept)(L1-acr)(CO)3] (pept=peptide; acr=acridine-based agent) in which the fac-[M(CO)3]+ moiety (1st function, M = 99mTc, Re) couples an acridine-based nuclear-targeting agent (2nd function, L1-acr) and the specific cell-receptor-binding peptide bombesin (3rd function, L2-pept). The metal-mediated coupling is based on the mixed ligand [2 + 1] principle. The nuclear targeting agents have been derivatized with an isocyanide group for monodentate (L1) and bombesin (BBN) with a bidentate ligand (L2) for complexation to fac-[M(CO)3]+. For nuclear uptake studies, the model complexes [Re(L2)(L1-acr)(CO)3] (L2 = pyridine-2-carboxylic acid and pyridine-2,4-dicarboxylic acid) were synthesized and structurally characterized. We selected acridine derivs. as nuclear-targeting agents, because they are very good nucleus-staining agents and exhibit strong fluorescence. Despite the bulky metal complexes attached to acridine, all [Re(L2)(L1-acr)(CO)3] showed high accumulation in the nuclei of PC3 and B16F1 cells, as evidenced by fluorescence microscopy. For radio-pharmaceutical purposes, the 99mTc analogs have been prepared and radio-activity distribution confirmed the fluorescence results. Coupling of BBN to L2 gave the receptor-selective complexes [M(L2-BBN)(L1-acr)(CO)3]. Whereas no internalization was found with B16F1 cells, fluorescence microscopy on PC3 cells bearing the BBN receptor showed high and rapid uptake by receptor-mediated endocytosis into the cytoplasm, but not into the nucleus.

OSC.G 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:554268 CAPLUS
DN 148:116045
TI Biological evaluation and comparison of three different procedures for labelling of amino acids tyrosine and lysine with technetium-99m
AU Djokic, D.; Jankovic, D.
CS Laboratory for Radioisotopes, The Institute of Nuclear Sciences "Vinca", Belgrade, 11001,
SO Journal of Labelled Compounds and Radiopharmaceuticals (2007), 50(3), 155-163
CODEN: JLCRD4; ISSN: 0362-4803
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB The 99mTc-labeling of the amino acids tyrosine (Tyr) and lysine (Lys), fundamental building blocks of proteins and peptides, as well as biol.

properties of the labeled compds. are investigated. Three different approaches for the labeling with ^{99m}Tc have been investigated: direct reduction with stannous tin in the presence of the amino acids, the preformed chelate approach through polydentate chelates DTPA and GH, and the 'organometallic approach' using $[\text{99mTc}(\text{CO})_3(\text{H}_2\text{O})_3]^+$ precursor. The direct labeling approach was not successful and the yield was poor. In the presence of DTPA and GH, the labeling efficiency was between 43.6 and 97.8%, depending on the amino acid and the polydentate chelate. The use of $[\text{99mTc}(\text{CO})_3(\text{H}_2\text{O})_3]^+$ precursor point at the formation of $^{99m}\text{Tc}(\text{I})$ coordinated complexes with high yield. In this approach, pH and heating influenced the yields. The results of organ distribution study for $[\text{99mTc}(\text{Tyr})(\text{H}_2\text{O})(\text{CO})_3]$ and $[\text{99mTc}(\text{Lys})(\text{H}_2\text{O})(\text{CO})_3]$ show accumulation in liver, kidneys and intestine.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2005:673310 CAPLUS

DN 143:165466

TI Metal complexes having vitamin B12 as a ligand

IN Alberto, Roger; Knight Castro, Hector Humberto; Mundweiler, Stefan

PA Universitaet Zuerich, Switz.; Kunze, Susanne Barbara

SO PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005068483	A1	20050728	WO 2005-EP168	20050110
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005205126	A1	20050728	AU 2005-205126	20050110
	CA 2552916	A1	20050728	CA 2005-2552916	20050110
	EP 1704157	A1	20060927	EP 2005-706857	20050110
	EP 1704157	B1	20090916		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	CN 1910192	A	20070207	CN 2005-80002150	20050110
	BR 2005006740	A	20070515	BR 2005-6740	20050110
	JP 2007518727	T	20070712	JP 2006-548244	20050110
	AT 443070	T	20091015	AT 2005-706857	20050110
	IN 2006CN02487	A	20070608	IN 2006-CN2487	20060706
	US 20090175775	A1	20090709	US 2006-585294	20060706
	KR 2007010119	A	20070122	KR 2006-713695	20060707
PRAI	EP 2004-75003	A	20040108		
	EP 2004-77937	A	20041025		
	WO 2005-EP168	W	20050110		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OS CASREACT 143:165466

AB The present invention relates to a metal complex $\text{M}(\text{L})_n$, wherein each L is independently selected and represents a ligand and at least one L is vitamin B12(cyanocobalamin) or a derivative thereof bound through the N atom

of its cyanide group to M, which is an element selected from the transition metals, thus, forming a M-NC-[Co] moiety with [Co] representing vitamin B12 without cyanide and wherein n is 1, 2, 3, 4, 5 or 6. The complex can be prepared by mixing a precursor mol. with vitamin B12. The metal complexes can be used for radiodiagnostics, chemotherapy and radionuclide therapy.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2005:11530 CAPLUS

DN 142:272777

TI Novel carbohydrate-appended metal complexes for potential use in molecular imaging

AU Storr, Tim; Obata, Makoto; Fisher, Cara L.; Bayly, Simon R.; Green, David E.; Brudzinska, Izabela; Mikata, Yuji; Patrick, Brian O.; Adam, Michael J.; Yano, Shigenobu; Orvig, Chris

CS Medicinal Inorganic Chemistry Group Department of Chemistry, University of British Columbia, Vancouver, BC, V6T 1Z1, Can.

SO Chemistry--A European Journal (2005), Volume Date 2004, 11(1), 195-203
CODEN: CEUJED; ISSN: 0947-6539

PB Wiley-VCH Verlag GmbH & Co. KGaA

DT Journal

LA English

OS CASREACT 142:272777

AB Seven discrete sugar-pendant diamines were complexed to the [M(CO)3]+ (99mTc/Re) core: 1,3-diamino-2-Pr β -D-glucopyranoside (L1), 1,3-diamino-2-Pr β -D-xylopyranoside (L2), 1,3-diamino-2-Pr α -D-mannopyranoside (L3), 1,3-diamino-2-Pr α -D-galactopyranoside (L4), 1,3-diamino-2-Pr β -D-galactopyranoside (L5), 1,3-diamino-2-Pr β -(α -D-glucopyranosyl-(1,4)-D-glucopyranoside) (L6), and bis(aminomethyl)bis[(β -D-glucopyranosyloxy)methyl]methane (L7). The Re complexes [Re(L1-L7)(Br)(CO)3] were characterized by 1H and 13C 1D/2D NMR spectroscopy which confirmed the pendant nature of the carbohydrate moieties in solution. Addnl. characterization was provided by IR spectroscopy, elemental anal., and mass spectrometry. Two analogs, [Re(L2)(CO)3Br] and [Re(L3)(CO)3Br], were characterized in the solid state by x-ray crystallog. and represent the first reported structures of Re organometallic carbohydrate compds. Conductivity measurements in H2O established that the complexes exist as [Re(L1-L7)(H2O)(CO)3]Br in aqueous conditions. Radiolabeling of L1-L7 with [99mTc(H2O)3(CO)3]+ afforded in high yield compds. of identical character to the Re analogs. The radiolabeled compds. exhibit high in vitro stability towards ligand exchange in the presence of an excess of either cysteine or histidine over a 24 h period.

OSC.G 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2004:836830 CAPLUS

DN 142:32081

TI Vitamin B12 as a ligand for technetium and rhenium complexes

AU Kunze, Susanne; Zobi, Fabio; Kurz, Philipp; Spingler, Bernhard; Alberto, Roger

CS Institute of Inorganic Chemistry, University of Zurich, Zurich, 8057, Switz.

SO Angewandte Chemie, International Edition (2004), 43(38), 5025-5029
CODEN: ACIEF5; ISSN: 1433-7851

PB Wiley-VCH Verlag GmbH & Co. KGaA

DT Journal

LA English
OS CASREACT 142:32081
AB Robust complexes with a central {Co-CN-Re(Tc)} feature are formed when the cyanide ligand in vitamin B12 acts as bridging ligand between Re and Tc carbonyl complexes. This concept paves the way for radiolabeling of vitamin B12 or metal-mediated coupling of bioactive mols. The crystal structures of 2 Re complexes were determined One of the Re complexes were characterized by cyclic voltammetry.

OSC.G 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2004:344666 CAPLUS

DN 141:81203

TI A new [2 + 1] mixed ligand concept based on [99(m)Tc(OH₂)₃(CO)₃]⁺: a basic study

AU Mundwiler, Stefan; Kuendig, Monika; Ortner, Kirstin; Alberto, Roger

CS Institute of Inorganic Chemistry, University of Zurich, Zurich, 8057, Switz.

SO Dalton Transactions (2004), (9), 1320-1328

CODEN: DTARAF; ISSN: 1477-9226

PB Royal Society of Chemistry

DT Journal

LA English

OS CASREACT 141:81203

AB Mixed ligand fac-tricarbonyl complexes [M(L₁)(L₂)(CO)₃] (M = Re, 99(m)Tc, L₁ = imidazole, benzyl isocyanide (bic), L₂ = 1H-imidazole-4-carboxylic acid (Himc), pyridine-2,4-dicarboxylic acid (2,4-dipicH₂), pyridine-2,5-dicarboxylic acid (2,5-dipicH₂)) were prepared starting from the precursors [M(OH₂)₃(CO)₃]⁺. The complexes can be obtained in good yield and purity in a two-step procedure by 1st attaching the bidentate ligand followed by addition of the monodentate. 99mTc compds. can also be prepared at the tracer level in 1-pot procedures with L₁ and L₂ being concomitantly present. This [2 + 1] approach allows the labeling of bioactive mols. containing a monodentate or a bidentate donor site. Examples are N-(tert-butoxycarbonyl)glycyl-N-(3-(imidazol-1-yl)propyl)phenylalaninamide and 5-((3-(imidazol-1-yl)propyl)aminomethyl)-2'-deoxyuridine as L₁ and N-((6-carboxypyridine-3-yl)methyl)glycylphenylalanine as L₂. The corresponding 2nd ligand can be used to influence the physicochem. properties of the conjugate. The crystal structures of [99Tc(OH₂)(imc)(CO)₃], [Re(OH₂)(2,4-dipic)(CO)₃], [Re(bic)(2,4-dipic)(CO)₃] and [Re(Im)(2,5-dipic)(CO)₃] are reported.

OSC.G 23 THERE ARE 23 CAPLUS RECORDS THAT CITE THIS RECORD (23 CITINGS)

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2001:265426 CAPLUS

DN 134:289554

TI Carbon monoxide source for preparation of transition metal carbonyl complexes

IN Alberto, Roger Ariel

PA Mallinckrodt Inc., USA

SO PCT Int. Appl., 16 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001025243	A1	20010412	WO 2000-EP9856	20001005

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2385927 A1 20010412 CA 2000-2385927 20001005
EP 1218385 A1 20020703 EP 2000-972700 20001005
EP 1218385 B1 20090107

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

HU 2002003138 A2 20021228 HU 2002-3138 20001005
HU 2002003138 A3 20031229
HU 226659 B1 20090629
JP 2003511334 T 20030325 JP 2001-528187 20001005
CN 1187359 C 20050202 CN 2000-813654 20001005
RU 2256664 C2 20050720 RU 2002-106404 20001005
AU 783079 B2 20050922 AU 2001-11344 20001005
IL 148971 A 20060705 IL 2000-148971 20001005
AT 420093 T 20090115 AT 2000-972700 20001005
ES 2320407 T3 20090522 ES 2000-972700 20001005
CZ 301030 B6 20091014 CZ 2002-1118 20001005
US 7053242 B1 20060530 US 2002-89036 20020325
US 20060030722 A1 20060209 US 2005-237374 20050928
PRAI EP 1999-203254 A 19991005
WO 2000-EP9856 W 20001005
US 2002-89036 A3 20020325

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OS CASREACT 134:289554; MARPAT 134:289554

AB The present invention relates to compds. that have a novel use as a carbon monoxide source and optionally as a reducing agent in the preparation of transition metal carbonyl complexes. The compds. are (X1)(X2)(X3)BC(O)Y where X1, X2 and X3 are the same or different and either a Lewis base or hydride and Y is a sigma donating group. The preparation of these compds. is described as is the use of H3BCO as a reducing agent. Thus, K2H3BCO2 was prepared by bubbling H3BCO through and ethanolic KOH solution K2H3BCO2 can be reacted with [99mTcO4]- to generate [99mTc(OH2)(CO)3]+.

OSC.G 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2000:608618 CAPLUS
DN 133:204807
TI Molecules for the treatment and diagnosis of tumors
IN Alberto, Roger Ariel; Schibli, Roger
PA Mallinckrodt Inc., USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000050086	A1	20000831	WO 2000-EP1553	20000224
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CA 2360419 A1 20000831 CA 2000-2360419 20000224
 CA 2360419 C 20090922
 EP 1154798 A1 20011121 EP 2000-910711 20000224
 EP 1154798 B1 20060510

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JP 2002537360 T 20021105 JP 2000-600696 20000224
 AT 325624 T 20060615 AT 2000-910711 20000224
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 US 20050019254 A1 20050127 US 2004-707994 20040130
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 PRAI US 1999-121340P P 19990224
 EP 1999-200754 A 19990312
 WO 2000-EP1553 W 20000224
 US 2001-913788 A1 20010815
 US 2004-707994 A1 20040130

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AB The invention relates to mols. for treatment and diagnosis of tumors and malignancies, comprising a tumor seeking biomol., which is coupled to an intercalating moiety, which is capable of complexing a metal, which metal is preferably a radioactive metal, to the use of these mols. and to therapeutic and diagnostic compns. containing them.

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RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2000:222269 CAPLUS

DN 133:55391

TI Influence of the Denticity of Ligand Systems on the in Vitro and in Vivo Behavior of ^{99m}Tc(I)-Tricarbonyl Complexes: A Hint for the Future Functionalization of Biomolecules

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AB Functionalization of biol. relevant mols. for the labeling with the novel fac-[^{99m}Tc(OH₂)₃(CO)₃]⁺ precursor has gained considerable attention recently. Therefore, we tested seven different tridentate (histidine L1, iminodiacetic acid L2, N-2-picolylamineacetic acid L3, N,N-2-picolylaminodiacetic acid L4) and bidentate (histamine L5, 2-picolinic acid L6, 2,4-dipicolinic acid L7) ligand systems, with the potential to be bifunctionalized and attached to a biomol. The ligands allowed mild radiolabeling conditions with fac-[^{99m}Tc(OH₂)₃(CO)₃]⁺ (30 min, 75 °C). The ligand concns. necessary to obtain yields of >95% of the corresponding organometallic complexes 1-7 ranged from 10⁻⁶ to 10⁻⁴ M. Complexes of the general formula "fac-[^{99m}TcL(CO)₃]" (L = tridentate ligand) and "fac-[^{99m}Tc(OH₂)L'(CO)₃]" (L' = bidentate ligand), resp., were produced. Challenge studies with cysteine and histidine revealed significant displacement of the ligands in complexes 5-7 but only little exchange with complexes 1-4 after 24 h at 37 °C in PBS buffer.

However, no decomposition to $^{99m}\text{TcO}_4^-$ was observed under these conditions. All complexes showed a hydrophilic character (log P_o/w values ranging from -2.12 to 0.32). Time-dependent FPLC analyses of compds. 1-7 incubated in human plasma at 37 °C showed again no decomposition to $^{99m}\text{TcO}_4^-$ after 24 h at 37 °C. However, the complexes with bidentate ligands (5-7) became almost completely protein bound after 60 min, whereas the complexes with tridentate coordinated ligands (1-4) showed no reaction with serum proteins. The compds. were tested for their in vivo stability and the biodistribution characteristics in BALB/c mice. The complexes with tridentate coordinated ligand systems (1-4) revealed generally a good and fast clearance from all organs and tissues. On the other hand, the complexes with only bidentate coordinated ligands (5-7) showed a significantly higher retention of activity in the liver, the kidneys, and the blood pool. Detailed radiometric analyses of murine plasma samples, 30 min p.i. of complex fac- $^{99m}\text{TcL1}(\text{CO})_3$, 1, revealed almost no reaction of the radioactive complex with the plasma proteins. By contrast, in plasma samples of mice, which were injected with complex fac- $^{99m}\text{Tc}(\text{OH}_2)\text{L5}(\text{CO})_3$ +, 5, the entire radioactivity coeluded with the proteins. On the basis of these in vitro and in vivo expts., it appears that functionalization of biomols. with tridentate-chelating ligand systems is preferable for the labeling with fac- $^{99m}\text{Tc}(\text{OH}_2)_3(\text{CO})_3$ +, since this will presumably result in radioactive bioconjugates with better pharmacokinetic profiles.

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